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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/020,063	12/13/2001	Kevin P. Baker	GNE.2830P1C65	9309

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EXAMINER	
BUNNER, BRIDGET E	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 10/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/020,063	**Applicant(s)** BAKER ET AL.	
	Examiner Bridget E. Bunner	**Art Unit** 1647	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 21 June 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *23 September 2005*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *33,38-40 and 44-47*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s).
13. ☐ Other: _____.

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Continuation of 5. Applicant's reply has overcome the following rejection(s): The objections to claims 33 and 38 are withdrawn in view of the amendment to claim 33 and Applicant's persuasive arguments.

Continuation of 11. does NOT place the application in condition for allowance because: Claims 33, 38-40, and 44-47 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Applicant's arguments (21 June 2005), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant asserts that the utility of the polynucleotide does not depend upon the function of the encoded protein. Applicant points out that a polynucleotide may have utility as a disese marker. Applicant argues that one of ordinary skill in the art would readily understand how to use a polynucleotide that is overexpressed in lung and colon tumor for the diagnosis of lung and colon cancer without necessarily knowing the function of the encoded protein. Applicant's arguments have been fully considered but are not found to be persuasive. In the instant case, the asserted utility that PRO1759 nucleic acids are useful as diagnostic markers for cancer is not substantial in that further research is required to reasonably confirm a real world context of use. In order for PRO1759 nucleic acid to be useful as a cancer diagnostic agent, there must be a detectable change in the amount or form of PRO1759 nucleic acid between cancerous and healthy tissue. In the instant case, the evidence of record indicates that the initial gene amplification assay only showed a positive result for three out of 52 lung and colon cancer samples, and did not take into account aneuploidy in cancerous and non-cancerous lung tissue (lack of matched tissue sample control, lack of aneuploidy control). In view of this, the skilled artisan would have viewed the gene amplification results as preliminary with respect to the utility of the claimed nucleic acids, and would have had to experiment further to reasonably confirm whether or not PRO1759 nucleic acids can be used as a cancer diagnostic agent.

At pages 10-12 and 15 of the Response, Applicant discusses the declaration of Dr. Goddard and Dr. Ashkenazi. Applicant has attached a copy of the return postcard stamped by the PTO indicating receipt of the declarations. Applicant reiterates that the declaration of Dr. Goddard and Dr. Ashkenazi should be considered. Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, although Applicant may have submitted the Goddard and Askenazi declarations, the Examiner cannot consider them because they are unable to be located and scanned into the instant application. The Examiner will be able to consider them if courtesy copies are submitted by Applicant. It is noted that the Examiner addressed Applicant's arguments regarding these declarations for reasons already made of record in the previous Office Action.

At pages 13-14 of the Response, Applicant asserts that Hu et al. does not conclusively show that it is more likely than not that the gene amplification does not result in increased expression at the mRNA and polypeptide levels. Applicant's arguments have been fully considered but are not found to be persuasive. Hu et al. analyzed 2286 genes that showed a greater than 1-fold difference in mean expression level between breast cancer samples and normal samples in a microarray (pg 408, middle of right column) and discovered that, for genes displaying a 5-fold change or less in tumors compared to normal, there was no evidence of a correlation between altered gene expression and a known role in the disease. However, among genes with a 10-fold or more change in expression level, there was a strong and significant correlation between expression level and a published role in the disease (see discussion section). The instant specification also does not demonstrate that the increased copy number of PRO1759 DNA in human lung tumors and colon tumors leads to an increased expression of PRO1759 polypeptide in these tumors. Therefore, since Applicants does not provide information regarding the level of expression, an activity, or a role in cancer or any other disease for the PRO1759 polypeptide, the polynucleotide and polypeptide lack a substantial utility or well established utility.

Applicant argues that it is known in the art that detection of gene amplification can be used for cancer diagnosis regardless of whether the increase in gene copy number results from intrachromosomal changes or from chromosomal aneuploidy. Applicant indicates that the gene amplification of a gene is useful as a diagnostic marker. Applicant also submits that Hittleman and Fleishhacker do not disclose aneuploid DNA in normal tissues or cells, but in tissue that has been damaged. Applicant's arguments have been fully considered but are not found to be persuasive. The instant specification does not assert that PRO1759 can be used as a precancer marker or as a cancer risk determining agent. The specification does not disclose whether PRO1759 gene is amplified, for example, only in lung tumor, or also in precancerous lung, or also in healthy lung. Given that proper controls were not done (i.e., comparing gene amplification levels between cancerous and non-cancerous matched tissues), and that PRO1759 was positive in only 3 out of 52 tumor samples, further research

would reasonably be required of the skilled artisan to confirm the utilities asserted in the specification. Such a requirement for further research indicates that the asserted utilities are not substantial.

Claims 33, 38-40, and 45-47 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicant states that a specific and substantial asserted utility has been disclosed, as described above. Specifically, since Applicant has not provided evidence to demonstrate that the PRO1759 polynucleotide and polypeptide have a specific and substantial asserted utility or a well established utility, one skilled in the art would not know how to use the claimed invention.